Appl. No. 09/822,585
Amdt. Dated August 14, 2003
Reply to Office Action of March 18, 2003

Docket No. MGH-004BUS

In the claims:

A full set of the pending claims showing markups is set forth below:

Please cancel Claims 31-38.

1. (Currently Amended) A method of forof measuring processing brain activity signals, the method comprising:

nonivasilvely noninvasively obtaining signals of central nervous system (CNS) activity from a subject;

localizing signals to specific anatomical and functional CNS regions which participate in reward/aversion functions;

correlating the signals in a reward/aversion brain region to a type of pain in the subject; and

interpreting the correlation results as an indication of the type of pain in the subject.

2. (Currently Amended) The method of Claim 1, wherein the reward/aversion regions areinclude at least one of the subcortical gray, brainstem, cerebellum and frontal brain regions.

3. (Original) The method of Claim 2 wherein the brainstem region includes the spinal cord.

4. (Original) The method of Claim 1 wherein the spinal cord includes the trigeminal nucleus and the method further includes the step of non-invasively obtaining signals from the trigeminal nucleus.

5. (Currently Amended) The method of Claim 13, wherein the reward/aversion regions include at least one of the orbital gyrus (Gob), ventral tegmentum/periaqueductal gray VT/PAG, nucleus accumbuems (NAc), sublenticular extended amygdala (SLEA), cingulate gyrus, primary somatosensory cortex (S1), secondary somatosensory cortex (S2), thalamus, insula, cerebellum,

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prefrontal cortex, amygdala, hypothalamus , parahippocampal gyrus, hippocampus, entorrhinal cortex, ventral pallidum, dorsal striatum, primary motor cortices (M1), secondary motor cortices (M2), M1, M2, supplementary motor cortex (SMA), frontal eye field (FEF), rostral ventralmedial medulla (RVM), and brainstem subnuclei.

6.      (Original) The method of Claim 1, wherein obtaining signals of CNS activity includes using a neuroimaging device wherein the signals reflect at least one of functional activation, chemical signatures, brain structure, neurotransmission, electromagnetic activity, perfusion effects and cell metabolism.

7.      (Currently Amended) The method of Claim 6, wherein the neuroimaging device corresponds to one or more of: a positron emission tomography (PET) device, ana functional magnetic resonance imaging (fMRI) device, ana magnetoencephalography (MEG) device, an electroencephgraphyelectroencephalography (EEG) device, a single photon emission computer tomography (SPECT) device, an infrared (IR) device, a magnetic resonance spectroscopy (MRS) device, and a functional computerized tomography (CT) device.

8.      (Original) The method of Claim 4, further comprising:
        aligning an imaging axis of an imaging device with the spinal cord of a subject such that the imaging axis is aligned in a plane parallel to a spinal cord axis and perpendicular to a cerebral mid-plane; and
        obtaining images of CNS regions in the spine.

9.      (Currently Amended) The method of Claim 1, wherein non-invasively obtaining signals of central nervous system obtained-non-invasivelyactivity further comprises:
        correcting the signals to reduce the effects of head motion;
        transforming the signals into a uniform atomic space;
        normalizing the transformed signals;
        statistically mapping the normalized signal; and

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locating the statistical maps over images reflecting at least one of: a uniform atomic space, an average anatomic space, and an individual atomic space.

10.    (Currently Amended) The method of Claim 1, wherein non-invasively obtaining signals of central nervous system obtained non-invasivelyactivity further comprises:

correcting the signals to reduce the effects of head motion;

aligning the signals with individual brain anatomy;

normalizing the transformed signals;

statistically mapping the normalized signal; and

locating the statistical maps over images reflecting at least one of: a uniform atomic space, an average anatomic space, and an individual atomic space.

11.    (Currently AmendedOriginal) The method of Claim 1, wherein correlating the signals from reward/aversionaversive brain regions comprises evaluating the temporal nature of a neuroimaging signal using waveform based correlation analysis (WCA).

12.    (Original) The method of Claim 11, wherein data obtained from central nervous system activity is segregated temporally.

13.    (Original) The method of Claim 12 wherein data obtained from central nervous system activity is segregated temporally into a plurality of phases.

14.    (Currently Amended) The method of Claim 12, wherein the step of temporally segregating includes the step of segregating into an early phase waveform and a late phase waveform.

15.    (Original) The method of Claim 13, wherein interpreting the results of the correlating procedure further comprises correlating a plurality of pixels from regions in the CNS to distinct waveforms.

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16. (Original) The method of Claim 15, wherein the distinct waveforms correspond to at least one of an early phase waveform and a late phase waveform.

17. (Original) The method of Claim 15, wherein interpreting the results of the correlating procedure further comprises producing indices by quantifying the signals using at least one of:

a spatial analysis;

a temporal analysis;

a comparison of slope analysis;

moment analysis;

laterality analysis;

synchrony analysis;

volume analysis;

power function used to generate indices;

power spectrum analysis used to generate indices;

integral analysis; and

derivative analysis.

18. (Currently Amended) The method of Claim 17, wherein interpreting the results of the correlating procedure further comprises using one or more quantitative indices wherein at least one of the one or more quantitative indices corresponds to one of:

a coordinate index from a uniform anatomic space;

a subregion index;

a subnuclear index;

a first time index $T_p$ corresponding to a first moment of a signal response;

a second time index $\Delta$ corresponding to a second moment of a signal response;

a rate of signal change index;

an average time of response index;

a width of response index;

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a tail index corresponding to a third moment of a signal response;

an R index;

an L index;

a fractional laterally index;

a correlation factor (r) index;

a volume index;

an exponent index;

an power spectrum index representing amplitudes of signal response harmonics and subharmonics computed using a power spectrum analysis;

an index corresponding to one or more amplitudes changes computed using an integral analysis of a signal response;

an index corresponding to a maximum rate of change of a signal response computed using a derivative analysis of a signal response; and

an index corresponding to a time to achieve a maximum rate of change of a signal response computed using a derivative analysis of the signal response.

19.    (Original) The method of Claim 1, further comprising:

providing a known first set of indices;

measuring one or more signal responses in a subject;

generating a second set of indices by computing one or more index for each of the one or more signal responses; and

comparing the second set of indices to the first set of indices.

20.    (Original) The method of Claim 19 wherein:

the step of providing the known first set of indices, includes the step of providing the known first set of indices to a processor; and

the step of comparing the second set of indices to the first set of indices includes the steps of:

providing the second set of indices to the processor; and

comparing the second set of indices to the first set of indices using the processor.

21.     (Original) The method of Claim 20 wherein the processor corresponds to a neural network processor.

22.     (Currently Amended) The method of Claim 1, further comprising:
        selecting an experimental process which elicits a response in one or more reward/aversion regions of a subject;
        applying a reward/aversive aversion stimulus to the subject to illicit the response; and
        correlating the experimental process to brain activity.

23.     (Original) The method of Claim 22, wherein the experimental process further comprises:
(a)     administering to the subject at least one of: a drug, a gene product, a biopharmaceutical, a virus, a gene, one or more receptors, and a neurochemical;
(b)     applying a stimulus to the subject; and
(c)     measuring a brain response of the subject.

24.     (Original) The method of Claim 23 further comprising measuring the response of the same subject over time.

25.     (Original) The method of Claim 24 wherein measuring the response of the same subject over time comprises the steps of waiting a period of time and repeating steps (a) – (c).

26.     (Currently Amended) The method of Claim 24 wherein measuring the response of the same subject over time comprises: the steps of
        waiting a period of time and performing the steps of:
(a)     administering a placebo to the subject;
(b)     applying a stimulus to the subject; and
(c)     measuring an analgesic response of the subject.

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27.    (Original) The method of Claim 22, wherein the experimental process comprises: exposing a subject to at least one of a thermal, mechanical or chemical stimulus; and measuring the response of the subject to the stimulus.

28.    (Original) The method of Claim 1, further comprising:

administering a treatment to the subject; and

correlating the treatment to brain activity.

29.    (Currently Amended) The method of Claim 2628, wherein the treatment corresponds to at least one of a drug/gene product, a surgical treatment, a radiation treatment, a behavioral treatment, and an acupuncture treatment.

30.    (Currently Amended) The method of Claim 1 wherein the step of interpreting the correlation result comprises:

correlating the signals from pain and reward brain regions; and

comparing results of the correlation to a predetermined index.

Claims 31-38 (Canceled)

39.    (New) A method of measuring pain in a subject comprising:

noninvasively obtaining signals of activity from at least two different reward/aversion regions of the CNS of the subject;

quantitating the signals to generate a pattern of activity; and

correlating the pattern to a degree or type of pain, thereby measuring pain in the subject.

40.    (New) The method of claim 39, wherein said reward/aversion regions are selected from the group consisting of: nucleus accumbems (NAc), sublenticular extended amygdala (SLEA), cingulate gyrus, primary somatosensory cortex (S1), secondary somatosensory cortex (S2),

thalamus, insula, cerebellum, prefrontal cortex, amygdala, hypothalamus, parahippocampal gyrus, hippocampus, entorrhinal cortex, ventral pallidum, dorsal striatum, primary motor cortices (M1), secondary motor cortices (M2), supplementary motor cortex (SMA), frontal eye field (FEF), rostral ventralmedial medulla (RVM), orbital gyrus (Gob), ventral tegmentum/periaqueductal gray (VT/PAG) and brainstem subnuclei.

41.    (New) A method of measuring pain in a subject comprising:

obtaining signals of activity from the nucleus accumbems (NAc) region of the brain of the subject;

quantitiating the signals to generate a pattern of activity; and

correlating the pattern to a degree or type of pain, thereby measuring pain in the subject.

42.    (New) A method for evaluating the efficacy of a treatment for pain comprising:

non-invasively obtaining signals of activity from at least two different reward/aversive regions of the CNS;

quantitiating the signals to generate a first pattern of activity;

administering a candidate treatment;

non-invasively obtaining signals of activity from the same at least two different reward/aversion regions of the CNS;

quantitiating the signals to generate a second pattern of activity; and

comparing the first and second patterns.

43.    (New) The method of claim 42, wherein one of the reward/aversion region is the NAc.

44.    (New) A method for evaluating the efficacy of a treatment for pain comprising:

non-invasively obtaining signals of activity from the nucleus accumbens (NAc);

quantitating the signals to generate a first pattern of activity;

administering a candidate treatment;

non-invasively obtaining signals of activity from the NAc;

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quantitating the signals to generate a second pattern of activity; and

comparing the first and second patterns.